

Translation

PATENT COOPERATION TREATY

PCT/JP2003/013932



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FP03-0298-00	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/013932	International filing date (day/month/year) 30 October 2003 (30.10.2003)	Priority date (day/month/year) 30 October 2002 (30.10.2002)
International Patent Classification (IPC) or national classification and IPC C12N 15/09, C12Q 1/68, G01N 33/50		
Applicant HISAMITSU PHARMACEUTICAL CO., INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input checked="" type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) <u>Disc 2</u> , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand 12 May 2004 (12.05.2004)	Date of completion of this report 08 June 2004 (08.06.2004)
Name and mailing address of the IPEA/IP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2003/013932

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ The international application as originally filed/furnished
- ☐ the description:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- pages _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) -- see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. excluding the subject matters concerning SEQ ID NOS: 1, 175 and 176

because:

- ☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. excluding the subject matters concerning SEQ ID NOS: 1, 175 and 176

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- | | | |
|----------------------------|--------------------------|-----------------------------------|
| the written form | <input type="checkbox"/> | has not been furnished |
| | <input type="checkbox"/> | does not comply with the standard |
| the computer readable form | <input type="checkbox"/> | has not been furnished |
| | <input type="checkbox"/> | does not comply with the standard |

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☒ see Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP03/13932

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-13	YES.
	Claims		NO
Inventive step (IS)	Claims	1-13	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Clin. Cancer Res., 2000, Vol. 6, No. 5, pages 1900-1908
 Document 2: Anticancer Res., 1998, Vol. 18, No. 2A, pages 1211-1215
 Document 3: Journal of Kyoto Prefectural University of Medicine, 1999, Vol. 108, No. 3, pages 381-388
 Document 4: Genome Res., 1998, Vol. 8, No. 11, pages 1097-1108, especially GenBank Database Accession No. AC093879

Claims 1-13

The subject matters of claims 1-13 appear to be novel and to involve an inventive step in view of documents 1-4 cited in the ISR.

Documents 1-3 describe specific genes having specific expression patterns in stage 4s neuroblastomas, but do not refer to the nucleic acid sequences represented by the SEQ ID NOS: 1, 175 and 176 of the present application. Furthermore, document 4 describes the human genome-derived sequence information including the nucleic acid sequences represented by the SEQ ID NOS: 1, 175 and 176 of the present application, but does not refer to the relationship with stage 4s neuroblastomas.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: III.1

The nucleic acids represented by SEQ ID NOS: 1-174 and the primers represented by SEQ ID NOS: 175-1076 respectively described in the claims are identical to each other only in the use for diagnosing/judging stage 4s neuroblastomas.

However, the following documents 1-3 describe specific genes having specific expression patterns in stage 4s neuroblastomas. Therefore, it is not considered a special technical feature in accordance with PCT Rule 13.2 to use specific genes having specific expression patterns in stage 4s neuroblastomas for diagnosing/judging stage 4s neuroblastomas.

In this case, according to PCT Rule 13.3, "The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim."

So, the nucleic acids represented by SEQ ID NOS: 1-174 and the primers represented by SEQ ID NOS: 175-1076 in the subject matters of the claims are not considered to be a group of inventions so linked as to form a single general inventive concept. Furthermore, in the relation between the nucleic acids represented by SEQ ID NOS: 1-174 and the corresponding pairs of primers, i.e., SEQ ID NOS: 175-518 and 1073-1076, each of the nucleic acids (174 inventions) satisfies the requirement of unity of invention, but the inventions concerning the other primers represented by SEQ ID NOS: 519-1072 are 554 independent inventions. So, it is considered that the claims describe 728 inventions in total.

Document 1: "High-level Expression of Angiogenic Factors Is Associated with Advanced Tumor Stage in Human Neuroblastomas," (A. Eggert, et al.), Clin. Cancer Res., 2000, Vol. 6, No. 5, pages 1900-1908

Document 2: "Differential Polymerase Chain Reaction with Serial Dilutions for Quantification of MYCN gene Amplification in Neuroblastoma," (S. Gallego, et al.), Anticancer Res., 1998, Vol. 18, No. 2A, pages 1211-1215

Document 3: Journal of Kyoto Prefectural University of Medicine, 1999, Vol. 108, No. 3, pages 381-388